

What is claimed is:

1. A solution formulation comprising:
 - (a) a physiologically tolerated mixed buffer system comprising TRIS combined with a buffering molecule which:
 - (i) absorbs carbon dioxide; and
 - (ii) does not contain a free amine group; and
 - (b) a polypeptide.
- 10 2. The formulation of claim 1, wherein the polypeptide is prone to aggregation.
3. The formulation of claim 1, further comprising zinc, wherein the zinc forms a stabilizing complex with the polypeptide.
4. The formulation of claim 1, further comprising a phenolic preservative.
5. The formulation of claim 1, wherein the buffering molecule is selected from the group consisting of acetate, phosphate and citrate.
- 20 6. The formulation of claim 5, wherein the buffering molecule is phosphate.
7. The formulation of claim 4 further comprising an isotonicity agent.
8. The formulation of claim 7, wherein the polypeptide is insulin.
- 25 9. The formulation of claim 8, wherein the insulin is a monomeric insulin analog selected from the group consisting of LysB28ProB29-human insulin and AspB28 human insulin.
10. The formulation of claim 8, wherein TRIS is present at a concentration of about 1.5 mg/ml to about 4.5 mg/ml; phosphate is present at a concentration of about 0.2 mg/ml to about 2.5 mg/ml, insulin is present at a concentration of about 250 to about 1000 U/ml, zinc is present at a concentration of about .07 μ g/ml to about .09 μ g/ml, m-cresol is present at a concentration of about

2.2 mg/ml, phenol is present at a concentration of about 0.9 mg/ml and glycerol is the isotonicity agent and is present at a concentration of about 16 mg/ml.

11. The formulation of claim 10, wherein TRIS is present at a concentration of about 2 mg/ml to
5 about 3 mg/ml and phosphate is present at a concentration of about 0.5 mg/ml to about 1.5 mg/ml.

12. The formulation of 8 for use in a continuous infusion system.

13. A method for treating diabetes comprising administering an effective dose of the formulation of
10 claim 8 to a patient in need thereof.

14. A method for treating diabetes comprising administering an effective dose of the formulation of
claim 8, wherein the formulation is administered using a continuous infusion system.

15. A method for treating hyperglycemia comprising administering an effective dose of the formulation
of claim 8 to a patient in need thereof.

16. The method of claim 15, wherein the formulation is administered using a continuous infusion
system.

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17. A stable, soluble formulation of insulin for use in a continuous infusion system, comprising: an
isotonicity agent; a mixed buffer system comprising TRIS combined with a buffer selected from the
group consisting of phosphate buffer, acetate buffer and citrate buffer; insulin; zinc; and a phenolic
preservative.

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18. A process for preparing the monomeric insulin analog formulation of claim 9 comprising the steps
of combining a physiologically-tolerated mixed buffer system comprising TRIS combined with a buffer
selected from the group consisting of phosphate buffer, acetate buffer and citrate buffer; with the
monomeric insulin analog; zinc; and a phenolic preservative.

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19. A method of stabilizing a polypeptide prone to aggregation comprising combining the peptide with
a physiologically-tolerated mixed buffer system comprising TRIS mixed with a buffering molecule that

does not contain a free amine group and which counteracts carbon dioxide; zinc; and a phenolic preservative.

20. The method of claim 19, wherein the buffering molecule is selected from the group consisting of
5 acetate, phosphate and citrate.

21. The method of claim 19, wherein the mixed buffer system further comprises an isotonicity agent.

22. The method of claim 19, wherein the polypeptide is a monomeric insulin analog selected from the
10 group consisting of LysB28ProB29-human insulin and AspB28 human insulin.

23. The method of claim 22, wherein TRIS is present at a concentration of about 1.5 mg/ml to about
4.5 mg/ml; phosphate is present at a concentration of about 0.2 mg/ml to about 2.5 mg/ml, the
monomeric insulin analog is present at a concentration of about 250 to about 1000 U/ml, zinc is
present at a concentration of about .07 μ g/ml to about .09 μ g/ml, m-cresol is present at a
concentration of about 2.2 mg/ml, phenol is present at a concentration of about 0.9 mg/ml and
glycerol is the isotonicity agent and is present at a concentration of about 16 mg/ml.

24. The method of claim 23, wherein TRIS is present at a concentration of about 2 mg/ml to about 3
mg/ml and phosphate is present at a concentration of about 0.5 mg/ml to about 1.5 mg/ml.

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